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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/300,612	04/27/1999	BINIE V. LIPPS	FWLPATU012	4662

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EXAMINER
BASKAR, PADMAVATHI

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/300,612	Applicant(s) LIPPS ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- Th MAILING DATE of this communication appears on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 7-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 7-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

1. Applicant's Appeal Brief filed on 3/14/03 (Paper # 21) is acknowledged.

Upon further review and consideration, the final rejection as set forth in the previous office action is hereby withdrawn. The amendment filed on 10/31/01 (Paper # 16) has been entered into the record. Claims 7-9 have been amended. Claims 5 and 7-16 are pending in the application.

2. In view of amendment to the claims, the rejection under 35U.S.C. 112, second paragraph is withdrawn.

3. The rejection of claims 5 and 7-16 under 35 U.S.C. 102(b) as being anticipated by Lipps et al US 5,744,449 is withdrawn because the inventors in the instant invention and the cited patent are identical.

Claim Objections

4. Claims, 5, 9, 11 and 14 recite specific amino acid sequences. However, the claims should include specific amino acid sequence by sequence identifier because the claims fail to satisfy the statute requirement. MPEP: 2422, 37 CFR 1.821 states that where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Therefore, applicant is advised to recite the SEQ ID NO in claims 5, 9, 11 and 14.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 5, 7-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5, 7 and 9 are rejected as being vague because it is not clear what is the purpose of this process? Or method? Is this process or method for detecting a toxin present in a sample obtained from animal plant or bacteria? or something else?

Claim 9 is rejected as being vague because it is not clear how neutralizing index is determined? Is this method a competitive ELISA assay for measuring the neutralization activity of anti-LTNF?

Claim 9 is also confusing how numerical assay values are predetermined? It is also clear whether first and second tests are performed individually or in the same assay? It is vague in reciting "toxin assay is determined by ELISA. Does applicant intend to mean the amount of toxin is determined by ELISA?

Claim 9 is vague and is not clear because how anti-LTNF reacts with free toxin in first test since first test uses normal serum?

Claim 15 recites the limitation "novel" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 15 is vague in reciting LTNF having non-immunological binding with toxin? It is not clear what is non-immunological binding means? Does applicant intend to mean that LTNF binds to toxin nonspecifically since LTNF does not precipitate with toxin and is not an immunoglobulin?

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 11- 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Sanchez et al 1998, Toxicon: 36: 1451- 1459 in light of Farah et al 1996, Toxicon: 34: 1067- 1071.

The claims are drawn to a composition of matter consisting essentially of an IgG antibody made against a peptide consisting of five to ten amino acids from the N-terminal sequence LKAMDPTPPLWIKTE in the absence of carrier protein molecule, said immunoglobulin selected from group consisting of an immunized animal serum, a hybridomas cell culture and a mouse ascitic fluid, said composition reacts immunologically with an animal toxin, a plant toxin and bacterial toxin.

Sanchez et al disclose a composition matter consisting essentially of a monoclonal antibody DV-2LD # 2 (see page 1453, Materials and Methods; under Monoclonal antibodies) made against anti-hemorrhagins.

The claimed LTNF / synthetic LTNF and the anti-hemorrhagins disclosed by Farah et al 1996 are same because the N-terminal sequence, LKAMDPTPPLWIKTE are same and found in the opossum serum (Figure 2, line 2 of Farah et al). Therefore, monoclonal antibodies disclosed by Sanchez et al read on the claimed composition.

Monoclonal antibody DV-2LD # reacted to anti-hemorrhagic proteins (see figure 1 (b).

These monoclonal antibodies are reacted with goat-anti-mouse IgG conjugated with horseradish peroxidase (see page 1455, top portion of the page) indicating that monoclonal antibodies are of IgG type. Monoclonal antibodies obtained after immunizing mice. Immunized mice spleen cells were fused to make hybridomas cell cultures (see page 1453, Materials and Methods; under Monoclonal antibodies). Further, the composition containing monoclonal antibody reacted in western blot assay to different snake venoms (see figure 1 b), said snake venom is a complex mixture of toxins (see figure 4 and page 1452, first paragraph under introduction). Thus the prior art anticipated the invention.

Claim Rejections - 35 USC 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 5, 7-8 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanchez et al 1998, Toxicon: 36: 1451- 1459 in view of Harlow and Lane 1988.

The claims are drawn to a process comprising contacting, in vitro, a biological toxin with an antibody made against N-terminal sequence LKAMDPTPPLWIKTE under conditions to cause the biological toxin to react immunologically with said antibody, said antibody reacts with a wide range of toxins, said reaction product is detected by ELISA.

Sanchez et al also teach a process, western blot assay (See page 1453, last paragraph through page 1454) comprising contacting a biological toxin from snake venom with a monoclonal antibody DV-2LD # 2 (see page 1453, Materials and Methods; under Monoclonal antibodies) made against anti-hemorrhagins comprising N-terminal sequence of LKAMDPTPPLWIKTE. Monoclonal antibody DV-2LD # reacted to anti-hemorrhagic proteins that bind to toxin (see figure 1 (b). Further, monoclonal antibody reacted in western blot assay to different snake venoms (see figure 1 b) said venom is a complex mixture of toxins (see figure 4 and page 1452, first paragraph under introduction). However, the prior art does not teach ELISA assay where anti-LTNF or Toxin is attached to the plate or double sandwich method.

Sanchez et al disclose a monoclonal antibody DV-2LD # 2 (see page 1453, Materials and Methods; under Monoclonal antibodies) to anti-hemorrhagic proteins comprising N-terminal sequence of LKAMDPTPPLWIKTE that bind to toxin. ELISA assays are well known in the art of immunology (Harlow and Lane 1988) in which either antigen or antibody is coated to the plate, ELISA double sandwich assay using two antibodies (page 579, 585 and 563) and measuring

the product of such reaction. ELISA immunoassays are routine in the art and are sensitive and specific because practically monoclonal antibodies are available for any antigen. These assays are so routine and kits are freely available in the market for detecting various antigens/ toxins since this assay does not need highly trained technical experts and could be used any place with minimum facilities. Therefore, It would have been obvious to a person of ordinary skill in the art at the time the invention was made to replace the western blot immunoassay as taught by Sanchez et al with ELISA assay using the same reagents disclosed by Sanchez et al as discussed above in paragraph # 7 with a reasonable expectation of success because it would have helped to reduce the laborious process involved in western-blot assay and more so the reagents are readily available for ELISA assay, which is less expensive and less time consuming. An artisan of ordinary skills would have been motivated in applying teaching of Sanchez et al to Harlow and Lane because Sanchez et al suggests that five step western-blot assay is sensitive and useful for determining hemorrhagic activity without using live animals to determine toxin activity (see page 1452lines 4-5) and might replace the animal bioassay. One of ordinary skill in the art would know how to use different ELISA assays using monoclonal antibodies to LTNF as disclosed by Sanchez et al. The claimed invention is prima facie obvious in view of Sanchez et al and Harlow and Lane absent any convincing evidence to the contrary.

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

7/10/03

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